In the United States Court of Federal Claims

No. 14-278V
(Filed: August 5, 2019)[1]

MELANIE YALACKI, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	)	Vaccine; Off-Table Injury; *Althen* Prong One; *Althen* Prong Two; Standard of Proof; Hepatitis B ("Hep B") Vaccine; Postural Orthostatic Tachycardia Syndrome ("POTS"); Chronic Fatigue Syndrome ("CFS"); Autoimmunity.

Richard Gage, Cheyenne, WY for petitioner. *Kristen L. Blume*, Cheyenne, WY of counsel.

Robert P. Coleman III, Torts Branch, Civil Division, United States Department of Justice, Washington, D.C., with whom were *Joseph H. Hunt*, Assistant Attorney General, *C. Salvatore D'Alessio*, Acting Director, *Catherine E. Reeves*, Deputy Director, and *Gabrielle M. Fielding*, Assistant Director, for respondent.

FIRESTONE, *Senior Judge*

O P I N I O N

Melanie Yalacki ("petitioner") seeks review of the Special Master's Decision Denying Entitlement ("Decision" or "Dec.") under the National Childhood Vaccine

[1] Pursuant to Rule 18(b) of the Vaccine Rules of the United States Court of Federal Claims, this opinion was initially filed under seal on July 15, 2019. The parties were to propose redactions of the information contained therein on or before July 29, 2019. No proposed redactions were submitted to the court.

Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 ("Vaccine Act" or "Act"), as amended. Mot. for Review ("MFR") (ECF No. 103). Specifically, petitioner challenges the Special Master's determination that petitioner did not adequately support her claim that a Hepatitis B ("Hep B") vaccination she received in June 2011 could have caused and did cause her to develop Postural Orthostatic Tachycardia Syndrome ("POTS") and Chronic Fatigue Syndrome ("CFS").[2]

Petitioner argues that the Special Master erred as a matter of law by imposing a burden of proof exceeding the preponderance of the evidence standard in the Act. MFR at 13. Petitioner argues that the Special Master erred by (1) allegedly requiring more than the concept of molecular mimicry along with some identified homology between an amino acid sequence and a target antigen under prong one of *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274 (Fed. Cir. 2005) ("*Althen*") and (2) requiring some evidence of an autoimmune response beyond the alleged injury under the second *Althen* prong. The Secretary of Health and Human Services ("the respondent" or the "government") responds that the Special Master identified the correct burden of proof by considering whether petitioner's theory was plausible under *Althen* prong one and

[2] POTS is a disease "marked by an increase in heart rate, or tachycardia, caused by a change in body position from the supine position to the upright position, without an accompanying increase in blood pressure." Dec. at 39 (citing R. Freeman, et al., *Consensus Statement on the Definition of Orthostatic Hypotension, Neurally Mediated Syncope and the Postural Tachycardia Syndrome*, 21 Clinical Autonomic Res. 69, 71 (2011)). CFS' "primary characteristic . . . is 'severe disabling fatigue,' which is accompanied by other symptoms including memory and concentration impairment, muscle pain, and impaired sleep." Dec. at 41 (quoting K. Fukuda, et al., *The Chronic Fatigue Syndrome: A Comprehensive Approach to Its Definition and Study*, 121 Annals of Internal Med. 953, 953 (1994)).

evaluating whether petitioner had provided evidence consistent with petitioner's proposed theory under *Althen* prong two. Resp. at 8 (ECF No. 107). For the reasons that follow, the court **DENIES** the petitioner's motion for review and **AFFIRMS** the Special Master's Decision.

I. BACKGROUND

A. Factual Background

The essential facts of this case are set forth in the Special Master's Decision, *see generally* Dec. at 2-11 (ECF No 102), and may be summarized as follows.

Prior to petitioner's receipt of the Hep B vaccine on June 2, 2011, petitioner had sought medical treatment for a wide array of issues, including dizziness, nausea, shakiness, fatigue, and muscle aches. Dec. 2-3. These same records reveal that petitioner also discussed mental health issues, including coping with anxiety, with physicians on numerous occasions throughout 2009 and 2010. *Id.* at 3 n.4.

On June 2, 2011, petitioner, who was then thirty-three years old, received her third Hep B vaccine. Dec. at 3. In the afternoon of June 2, 2011, hours after having received the vaccine, petitioner began to report that she "felt bad[,]" which included body aches and fatigue. *Id.* Petitioner attributed her feeling bad to the Hep B vaccine. *Id.* at 3-4. The next day, petitioner was examined by the doctor who had administered the Hep B vaccine. *Id.* at 4. The exam showed a normal result with no evidence of muscle weakness. *Id.*

Within the first month of receiving the Hep B vaccine, petitioner went to several doctors. *See* Dec. at 4-6. During these visits, multiple medical professionals informed petitioner that "(a) they could not identify the source of her symptoms, and (b) they did not deem it likely that the vaccine was causal of those symptoms." *Id.* at 5. This included an infectious disease specialist who told petitioner that the Hep B vaccine was not likely the source of her symptoms. *Id.* The infectious disease specialist also noted that petitioner's blood work revealed no other problems. *Id.*

At a consultation with Julie Cohen, M.D., on July 8, 2011, petitioner added cognitive delay, difficulty remembering basic words, and fainting to her symptoms. Dec. at 6. On July 11, 2011, petitioner called Dr. Cohen's office and stated that she believed she was suffering from CFS. *Id.* On July 28, despite petitioner's complaints, Dr. Cohen concluded that petitioner did not have CFS. *Id.*

Next, petitioner sought treatment with cardiologist Joseph Abruzzo, M.D., on September 8, 2011. Dec. at 6. Dr. Abruzzo felt that petitioner was potentially experiencing a "[s]yndrome of autonomic neuropathy" that was temporally associated with the Hep B administration. *Id.* at 6-7. Dr. Abruzzo performed a tilt table test on September 20, 2011, to test for POTS. *Id.* at 7. He concluded that the test did not reveal any evidence of autonomic dysfunction. *Id.*

On September 20, 2011, petitioner had a rheumatologic work-up to evaluate athralgias (joint pain) allegedly present since the Hep B vaccination, and the work-up resulted in no evidence of any joint inflammation or damage, and no signs to suggest

inflammatory arthritis, connective tissue disorder, or evidence of a serum sickness-like disorder. Dec. at 7 n.11. Petitioner visited a new primary care physician ("PCP"), Anisa Moore, M.D., on September 27, 2011, who diagnosed petitioner with CFS, despite a normal examination and without appearing to have reviewed petitioner's records. *Id.* at 7. When Dr. Moore emphasized treating petitioner's condition over identifying the cause of it, petitioner and her husband became angry and questioned Dr. Moore's competence to opine on causation. *Id.* at 8 n.13. By January 2012, petitioner visited another PCP, Andrea Fedele, M.D., who confirmed the CFS diagnosis based on petitioner's report of symptoms. *Id.* at 8. Dr. Fedele added that petitioner's CFS was "most consistent by history as due to the vaccination received on 6/2/2011." *Id.* Other physicians at further medical visits were not able to confirm petitioner's CFS diagnosis. *Id.* at 9.

Petitioner continued to seek additional treatment from other physicians, including neurologist Karen Rollins, M.D. Dec. at 9. Dr. Rollins, in contrast to Dr. Fedele, recorded her expansive review of petitioner's medical history after vaccination and opined that petitioner did not have POTS, her symptoms were not related to her June 2011 vaccination, and further treatment was unnecessary. *Id.*

In March 2013, petitioner visited another cardiologist, Adam Betkowski, M.D. Dec. at 9. Dr. Betkowski took note of petitioner's negative tilt table test results and performed his own in-clinic check of blood pressure and heart rate. *Id.* Dr. Betkowski determined that the changes in her blood pressure and heart rates were enough to "suggest possibly [POTS] with possibly borderline orthostatic hypertension." *Id.* at 9-10.

Also in March, petitioner's plasma norepinephrine levels were tested, and the test revealed that petitioner's plasma norepinephrine levels were normal. *Id*. at 10.

In the spring of 2014, almost three years after vaccination, petitioner visited Robert Gillespie, M.D. Dec. at 10. Petitioner informed Dr. Gillespie that she had been diagnosed with POTS, and he therefore, attempted to confirm the diagnosis. *Id.* On April 18, 2014, at petitioner's first visit with Dr. Gillespie, he performed a sit-stand test, which showed that petitioner's heart rate increased by twenty-eight beats per minute ("BPM") while her blood pressure remained unchanged. *Id*. Based on petitioner's self-reported history and the sit-stand test results, Dr. Gillespie diagnosed petitioner with POTS. *Id*. He was, however, unfamiliar with the idea that a vaccine could cause such a condition. *Id*. At petitioner's second visit with Dr. Gillespie on May 22, 2014, petitioner's heart rate was measured to have increased by seventeen BPM during a sit-stand test, while her blood pressure remained stable. *Id*. Dr. Gillespie reiterated his opinion that petitioner had POTS. *Id.*

Finally, in July 2014, petitioner went to another cardiologist, Elizabeth Noll, M.D. Dec. at 11. Dr. Noll's "assessment accepted the prior POTS diagnosis . . . but she acknowledged that other testing did not support the diagnosis" and that the 2011 tilt table test was inconclusive and should be repeated. *Id.*

B. Proceedings Before The Special Master

On April 10, 2014, petitioner filed a Petition for compensation under the Vaccine Act. Dec. at 1. Petitioner alleged that she suffered from CFS and/or POTS as a result of

receiving the Hep B vaccine on June 2, 2011. *Id.* In support of her position, petitioner filed five expert reports from Yehuda Shoenfeld, M.D., an internist and clinical immunologist, who opined that the Hep B vaccine caused petitioner's POTS by a process of molecular mimicry. *Id.* at 15. Dr. Shoenfeld's theory of molecular mimicry involves his contention that sequential/structural similarities between peptide amino acid sequences within the viral protein components of vaccines and self protein structures in the human body cause antibodies produced in response to a vaccine to mistakenly attack the self structures. *Id.* at 18. As applied here, Dr. Shoenfeld opined that a particular peptide sequence in the Hep B vaccine, LLLCL, had a homology with nerves. *Id.* Dr. Shoenfeld theorized that the antibodies could cause POTS when the antibodies interfere with the norepinephrine transporter which plays a role in regulating the orthostatic reaction and through this mechanism can cause higher blood norepinephrine levels. *Id.* at 19.

Part of Dr. Shoenfeld's proposed causation theory was based on his view that POTS is a "classic autoimmune disease" that could be caused by a vaccine. *Id.* at 16. In characterizing POTS as autoimmune, Dr. Shoenfeld stated that POTS reflects the working of the autonomic nervous system and that several triggers can bring about POTS including vaccines containing adjuvants. Dec. at 16. In his opinion, the autoimmune nature of POTS is supported by "several papers" including a paper published in 2007 which hypothesized that a particular autoantibody was associated with neuropathic cases of POTS. *Id.* at 17-18 (citing M. Thieben, et al., *Postural Orthostatic Tachycardia*

Syndrome: The Mayo Clinic Experience, 82 Mayo Clinic Proc. 308 (2007) ("Thieben Paper")). The Thieben Paper, however, did not propose that POTS is always an autoimmune disease. *Id.* at 18.

With regard to CFS, Dr. Shoenfeld conceded that CFS is not widely considered to be autoimmune and that no pathogenic autoantibodies have been identified in relation to CFS. Dec. at 19. He stated that he expects such autoantibodies will be discovered eventually. *Id.*

Dr. Shoenfeld concluded based on the foregoing that because petitioner had CFS together with POTS, these illnesses were strong evidence that petitioner experienced and was continuing to experience an autoimmune reaction to the Hep B vaccine. *Id.* at 17.

Respondent answered Dr. Shoenfeld's theory with reports from three expert witnesses. The first, Philip A. Low, M.D., is a neurologist who has treated many patients with POTS, CFS, orthostatic intolerance, autoimmune disorders, and autoimmune neuropathies. Dec. at 22. Dr. Low has co-authored over four hundred items of literature in the field of autoimmunity, including many articles on POTS, antibody-mediated autoimmune neuropathy, and orthostatic intolerance. *Id.*

Dr. Low stated that POTS is not usually caused by damage to the autonomic nervous system. Dec. at 22. Dr. Low opined that the Thieben Paper, referenced by Dr. Shoenfeld and co-authored by Dr. Low, indicated that where the patients observed tested positive for an antibody that is associated with a form of autonomic neuropathy and had POTS-like symptoms, the patients also had other accompanying symptoms such as loss

of bladder control, loss of ability to breath, and tissue injury. *Id.* at 23. Dr. Low stated that the medical record of this petitioner did not include any evidence that she experienced any of these accompanying symptoms. *Id.* Dr. Low further explained that that since the Thieben Paper was published, the researchers at the Mayo Clinic, looking more closely at the relationship between the autoantibodies and POTS, found "zero relationship of titer to autoimmune failure." *Id.* Based on this research, Dr. Low stated that he does not routinely test POTS patients for autoantibodies. *Id.* Dr. Low also stated that he saw no evidence in petitioner's medical record to support a conclusion that petitioner suffered from an autoimmune-mediated autonomic neuropathy that could have caused her POTS symptoms. *Id.* at 25-26.

Finally, Dr. Low addressed petitioner's reliance on the norepinephrine transporter malfunction as the cause of her POTS. Dec. at 26. Dr. Low explained that norepinephrine transporter malfunction resulting in excess norepinephrine in the blood is unlikely here where petitioner's blood norepinephrine levels were tested in 2013 and found normal. *Id.*

Respondent's second expert, Peter D. Donofrio, M.D., a neurologist, opined that with regard to petitioner's claim that she suffered from CFS, that he did not find anything in her medical record supporting a CFS diagnosis. Dec. at 27. Dr. Donofrio explained that petitioner's post-vaccination symptoms were likely caused by preexisting health problems and anxiety. *Id.*

Respondent's third expert, J. Lindsay Whitton, M.D., Ph.D., an immunologist, opined that Dr. Shoenfeld's theory that the Hep B vaccine could cause CFS or POTS was

scientifically unreliable. Dec. at 29. Dr. Whitton first challenged Dr. Shoenfeld's conclusion that the Hep B vaccine could cause an autoimmune response of some kind resulting in disease. *Id.* at 30. Dr. Whitton explained that "molecular mimicry" applies only to cases where a disease is observed, and he cautioned that it is wrong to assume that homology between antigen components and a self-protein will invariably result in harm. *Id*. He provided references to literature confirming that homology was "commonplace." *Id.* Dr. Whitton also testified that the peptide Dr. Shoenfeld had identified as most likely the source of petitioner's alleged autoimmune response was "cherry picked for this case," amounting to selection bias rather than verifiable evidence. *Id.*

Dr. Whitton opined that to reliably link the Hep B vaccine with POTS or CFS, he would require "proof of (a) the relevant autoantibody, (b) evidence of [petitioner]'s norepinephrine transporter protein dysfunction, or (c) some kind of experimental study or model establishing that the Hep B vaccine had been associated with the injuries alleged." Dec. at 31. He noted that Dr. Shoenfeld had not presented any such evidence. *Id.* Dr. Whitton stated that petitioner's normal plasma norepinephrine test results were inconsistent with petitioner's theory. *Id.* at 30.

The entitlement hearing was held on January 22-23, 2018. Dec. at 32. Dr. Shoenfeld, Dr. Low, Dr. Donofrio, and Dr. Whitton each testified, as well as petitioner's treating physicians, Dr. Fedele, and Dr. Gillespie, and petitioner herself. *Id*. at 11-31.

Ten months after the hearing, and three months after the parties filed post-hearing briefs, petitioner filed a sixth report from Dr. Shoenfeld, along with three pieces of

literature. Dec. at 15 n.17. Dr. Shoenfeld sought with this sixth report to respond to Dr. Whitton's criticism by offering evidence of other peptides that could cause the autoimmune reaction Dr. Shoenfeld associated with POTS. While Dr. Shoenfeld originally identified only the peptide LLLCL, in the sixth report he opined that a different peptide, STIPPA, can also be associated with an autoimmune response.

The Special Master, issued an order striking the sixth report on December 7, 2018, in which he explained that even if the assertions in Dr. Shoenfeld's sixth expert report were accepted as true, the assertions would not provide evidence that "any components of the Hep B vaccine *could* initiate any autoimmune or otherwise aberrant immune response sufficient to cause CFS or POTS." Dec. at 15 n.17 (emphasis in original). The Special Master also explained that the report was "(a) untimely, (b) not filed with [the Special Master's] permission or at [his] request, and (c) was not based on newly-discovered or published literature that could *itself* not have been filed in a timely fashion." *Id*. (emphasis in original).

On January 31, 2019, the Special Master issued his Decision Denying Entitlement. The Special Master summarized his determination as follows:

> Petitioner has not offered a reliable theory explaining how the Hep B vaccine could cause either of her alleged injuries. In addition, there are legitimate questions as to whether Petitioner actually suffered from CFS or POTS—but assuming that she did, the medical record does not support the conclusion that the vaccine likely caused either injury. The vaccination at issue was simply too remote in time from the record evidence most supportive of either diagnosis, while the symptoms she points to that occurred closer in time to vaccination either do not support her alleged injuries or can be explained by her pre-vaccination medical history.

Dec. at 2. This motion for review followed. The court heard oral argument on July 2, 2019.

II. LEGAL STANDARDS

A. Legal Standards of Proof Under the Vaccine Act

Under the Vaccine Act, a petitioner with a non-Table claim, like the claim at issue here, may receive compensation by proving that her injury was actually caused by a covered vaccination. 42 U.S.C. § 300aa-11(c)(1)(C)(ii). Specifically, a petitioner asserting a non-Table claim, must satisfy three elements established by the Federal Circuit in *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005) to receive compensation. These elements are now known as the "*Althen* prongs." Under *Althen*, to establish a prima facie case for actual causation, petitioner must "show by preponderant evidence that the vaccination brought about [the] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 (Fed. Cir. 2010) (citing *Althen*, 418 F.3d at 1278), *reh'g denied*, (Fed. Cir. 2010) (the three *Althen* prongs). "[E]ach prong of the *Althen* test is decided relative to the injury[.]" *Broekelschen v. Sec'y of Health and Human Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010).

Under the first *Althen* prong a petitioner must provide "a reputable medical theory[,]" *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir.

2006) (citation omitted), to show that the vaccine in question "can cause" the injury suffered, *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1326 (Fed. Cir. 2006) (citation omitted). A reputable medical or scientific explanation can be "evidence in the form of scientific studies or expert medical testimony[.]" *Althen*, 418 F.3d at 1278 (citation omitted). "Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case[.]" *Broekelschen*, 618 F.3d at 1345. "Although *Althen* and *Capizzano* make clear that a claimant need not produce medical literature or epidemiological evidence to establish causation under the Vaccine Act, where such evidence is submitted, the special master can consider it in reaching an informed judgment as to whether a particular vaccination likely caused a particular injury." *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1379 (Fed. Cir. 2009). The "assessment of whether a proffered theory of causation is 'reputable' can involve assessment of the relevant scientific data . . . from the vantage point of the Vaccine Act's preponderant evidence standard[.]" *Id.* at 1380. In considering whether a theory is reputable the special master may also consider the evidence submitted by the respondent. *See de Bazan v. Sec'y of Health and Human Servs.*, 549 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case in chief.").

To satisfy the second *Althen* prong, a petitioner must show the vaccine "did cause" the injury identified. *Andreu*, 569 F.3d at 1367. This means demonstrating "a logical

sequence of cause and effect showing the vaccination was the reason for the injury." *Doe v. Sec'y of Health and Human Servs*., 601 F.3d 1349, 1351 (Fed. Cir. 2010). For this prong, the special master may weigh the views of treating physicians against other, as well as contrary evidence present in the record. *Hibbard v. Sec'y of Health and Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for the special master to weigh competing physicians' conclusion against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012).

In evaluating expert testimony, special masters are charged with evaluating the reliability of expert testimony. "Assessments as to the reliability of expert testimony often turn on credibility determinations, particularly in cases such as this one where there is little supporting evidence for the expert's opinion." *Moberly*, 592 F.3d at 1325-26. The Federal Circuit has expressly found that "[f]inders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence." *Id*. at 1326.

B. Standard of Review of Special Master's Decision

The Court of Federal Claims may set aside a special master's finding of fact or conclusions of law only if they are shown to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 42 U.S.C. § 300aa-12(e)(2)(B). Rules of the United States Court of Federal Claims ("RCFC"), App. B, Vaccine Rule 27(b). Under established precedent, this court does "not reweigh the factual evidence,

assess whether the special master correctly evaluated the evidence, or examine the probative value of the evidence or the credibility of the witnesses – these are all matters within the purview of the fact finder." *Porter v. Sec'y of Health and Human Servs.*, 663 F.3d 1242, 1249 (Fed. Cir. 2011) (citing *Broekelschen*, 618 F.3d at 1349). As long as "the [S]pecial [M]aster has considered the relevant evidence," "drawn plausible inferences," and stated "a rational basis for the decision," reversible error is extremely difficult to establish. *Hines v. Sec'y of Health and Human Servs.*, 940 F.2d 1518, 1528 (Fed. Cir. 1991); *see Cedillo v. Sec'y of Health and Human Servs.*, 617 F.3d 1328, 1338 (Fed. Cir. 2010) (holding that if the Special Master's findings of fact are "based on evidence in the record that [is] not wholly implausible" this court must find the finding as not arbitrary and capricious). Indeed, arguments that "various pieces of evidence should have been given more or less weight by the special master . . . do not demonstrate reversible error" especially where witness credibility is involved. *Hines*, 940 F.2d at 1527.

III. DISCUSSION

Petitioner argues that the Special Master applied the wrong legal standard under *Althen* prong one and "imposed a burden far exceeding the preponderance standard." MFR at 13. Petitioner argues that the Special Master's application of a heightened burden "is most obvious" in the Special Master's evaluation of petitioner's reliance on molecular mimicry to show that Hep B can cause POTS. *See* MFR at 14. Petitioner argues that the Special Master made an error of law when he stated with regard to *Althen* prong one that "it is not enough for a claimant to invoke the concept of molecular mimicry along with

some identified homology between an amino acid sequence and a target antigen in order to carry her burden." Oral Arg. 11:14:14-11:15:07 (citing Dec. at 44). Petitioner also argues that the Special Master improperly "raised the burden of proof" in his application of *Althen* prong two by requiring proof that petitioner had an autoimmune response to the Hep B vaccine in the form of lab tests showing the presence of antibodies or demonstrating inflammation. MFR at 16 (citing Dec. at 46, 52).

The respondent contends that the Special Master applied the correct burden of proof for *Althen* prong one and justifiably concluded that petitioner had not produced sufficient evidence of a mechanism that could connect Hep B to POTS. The respondent also contends that the Special Master did not raise petitioner's burden of proof regarding *Althen* prong two and rationally concluded based on the evidence in the record that there was no evidence to support petitioner's claim that she had an autoimmune response to the Hep B vaccine that resulted in POTS or CFS. Finally, the respondent argues that the Special Master properly applied the evidentiary standards associated with *Althen* prong three and rationally concluded that petitioner failed to satisfy *Althen* prong three regarding the on-set of her claimed POTS and CFS. [3] For the reasons that follow, the

[3] Petitioner does not challenge the Special Master's findings under the third *Althen* prong in her Motion for Review. *See* Dec. at 48 ("Petitioner's claim also fails on her inability to establish that her POTS . . . began in a medically-acceptable timeframe in relation to her June 2011 vaccination"); *id*. at 52 (same for petitioner's CFS claim). However, at oral argument petitioner explained that the Special Master's alleged errors under *Althen* prongs one and two "poisoned the well" for the rest of the analysis. Oral Arg. 11:46:30-11:46:54.

court finds that the Special Master applied the appropriate burden of proof and that his decision is rationally supported by the record.

A. Summary of Special Master's Findings

1. The Special Master's Findings and Conclusions for the First *Althen* Prong

For *Althen* prong one, the Special Master stated "petitioners must provide a 'reputable medical theory,' demonstrating that the vaccine received *can cause* the type of injury alleged." Dec. at 34 (quoting *Pafford*, 451 F.3d at 1355-56). He explained that petitioners may satisfy the prong "without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory." *Id.* (citing *Andreu*, 569 F.3d at 1378-79). The Special Master emphasized that petitioners' medical evidence should be assessed in light of the Vaccine Act's preponderance standard, not evaluated for scientific certainty, and added that "special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury." *Id.* (citations omitted).

The Special Master began evaluating the first *Althen* prong by assessing the credibility and reliability of the expert evidence regarding whether the Hep B vaccine can cause POTS. The Special Master found that, in response to petitioner's experts, the respondent provided countervailing evidence with multiple experts, including Dr. Low who "happens to be one of the foremost authorities on the autonomic nervous system in the United States if not the world." Dec. at 43. The Special Master found that petitioner's expert, Dr. Shoenfeld, was not persuasive. *Id.* The Special Master stated that Dr.

Shoenfeld relied heavily on general theories and offered broad "blanket assertions" regarding the prevalence of autoimmunity and its link to vaccines. *Id.* Dr. Shoenfeld had "previously testified unpersuasively before on the same topic, and whose expertise on the immune system and autoimmunity in general was not accompanied by comparable expertise in treating or studying POTS and CFS." *Id.*

The Special Master also found Dr. Shoenfeld to be combative and evasive in answering to respondent's questions at the hearing. The Special Master noted Dr. Shoenfeld exhibited this behavior when answering questions regarding a paper he wrote but later retracted and when asked about his apparent service on the advisory board of an anti-vaccination group and that anti-vaccination group's apparent funding of some of his research. Dec. at 15-16 n.18. In view of the foregoing, the Special Master found that Dr. Shoenfeld had also "demonstrated biases and deficiencies (not to mention the apparent misrepresentations on his CV pointed out at hearing by Respondent)." *Id.* at 43. For these reasons, the Special Master decided "to give less weight overall to his pronouncements about POTS and its causes than to the testimony of Respondent's experts, who together provided a comprehensive and more persuasive picture of the condition at issue and the low likelihood that a vaccine could instigate it." *Id*.

The Special Master explained that even if he had found Dr. Shoenfeld to be more credible or persuasive, he would still have found petitioner's causation theory attempting to link the Hep B vaccine to POTS deficient in two respects. Dec. at 44. First, the Special Master described the testimony of Dr. Low, "whose direct experience studying the

etiology of POTS far outweighed Dr. Shoenfeld's," and who convincingly explained that it is unlikely that POTS is autoimmune in nature. *Id.* Dr. Low was a co-author of the Thieben Paper Dr. Shoenfeld relied on to suggest POTS is autoimmune in nature, but he explained that knowledge on the topic has evolved over time, and that presently he does not test for autoantibodies in most POTS patients, and does not treat POTS patients with immune system suppression methods. *Id*. The Special Master found the "remaining scientific evidence offered by Petitioner suggesting the POTS is typically autoimmune was thin" because it relied on "single case reports" or only offered an indirect connection between autoimmunity and conditions like POTS. *Id.*

Second, the Special Master further found that "even if it is granted that some rare forms of POTS *are* autoimmune in origin, there remain substantial deficiencies in Petitioner's theory that the Hep B vaccine could trigger a pathogenic process resulting in such an autoimmune attack leading to POTS." Dec. at 44. The Special Master stated that Dr. Whitton's testimony undermined petitioner's proposed theory. *Id*. at 44-45. The Special Master relied on Dr. Whitton's testimony that Dr. Shoenfeld's proposed amino acid sequence homology was of little consequence. *Id*. First, the Special Master explained that Dr. Whitton persuasively noted that the homology identified by Dr. Shoenfeld was cherry-picked in order to support petitioner's theory, as opposed to having been discovered while studying POTS and its causes. *Id*. at 45. In this connection, Dr. Whitton explained that the homologous sequences identified by petitioner "amounted to selection bias rather than verified and reliable scientific evidence of a pathologic cross-reaction

spurred by molecular mimicry." *Id.* at 30. Second, the Special Master explained that Dr. Whitton had convinced him that portions of petitioner's theory are speculative. *Id.* at 45. Where petitioner proposed that the Hep B vaccine can cross-react with norepinephrine transporter proteins and produce autoantibodies, *id.* at 44, the Special Master stated that Dr. Whitton had established "that the evidence that the norepinephrine transporter protein is the target antigen for autonomic nervous system interference sufficient to result in POTS is undeveloped," *id.* at 45.

Thus, the Special Master stated that invoking the theory of molecular mimicry with simply some identified homology is insufficient here to satisfy petitioner's burden under *Althen* prong one where a disease like POTS, which is not necessarily autoimmune is at issue. In such circumstances, the Special Master explained that "a petitioner needs to cite evidence, circumstantial or otherwise, suggesting a reason to find it plausible that the proposed autoimmune cross-reaction triggered by the relevant vaccine does occur." *Id.* at 44. While the Special Master conceded that petitioner offered some evidence for the proposed theory, he stated "the evidence [petitioner] offered connecting the Hep B vaccine to POTS was speculative, limited, or rebutted, and she could not breathe life into it with Dr. Shoenfeld's *ipse dixit* pronouncements on topics about which he knew demonstrably less." *Id.*

With regard to CFS, the Special Master stated that petitioner's theory "had many of the same weaknesses as her arguments associating POTS to the Hep B vaccine," but assumed without finding that "CFS can be caused by the Hep B vaccine."[4] *Id.* at 50 n.34.

2. The Special Master's Findings and Conclusions Under *Althen* Prong Two

With regard to *Althen* prong two, the Special Master explained that there must be "proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records" to establish the vaccine caused the claimed injury. Dec. at 35 (citing *Althen*, 418 F.3d at 1278). The Special Master further explained that "[i]n establishing that a vaccine 'did cause' injury, the opinions and views of the injured party's treating physicians are entitled to some weight." *Id.* (quoting *Andreu*, 569 F.3d at 1367). However, the Special Master stated that "views of treating physicians should also be weighed against each other, contrary evidence also present in the record – including conflicting opinions among such individuals." *Id.* (citation omitted).

Under this standard, the Special Master first considered whether petitioner had established by a preponderance of the evidence that she had POTS. The Special Master "could not conclude" that petitioner "actually ever had (or today has) POTS." Dec. at 45; *see also id*. at 48. While petitioner demonstrated "clinical indicia of POTS, such as

[4] The Special Master stated that "[b]ecause of the massive deficiencies in Petitioner's *Althen* prong two showing, she would not prevail even if I *did* find that she offered a plausible causation theory associating the Hep B vaccine with CFS" and therefore did "not include in this discussion a lengthy discussion of the strength of her *Althen* prong one showing with respect to CFS[.]" Dec. at 50 n.45.

dizziness and fatigue," her medical record indicated that she had also experienced these symptoms before her Hep B vaccination. *Id.* at 45. He stated that while some treaters concluded that petitioner had POTS, "an equal number of treaters ruled out POTS or doubted its diagnostic veracity – and they did so on the basis of better testing evidence." *Id.* at 46.

But even assuming petitioner had POTS, the Special Master determined that petitioner had not met her burden because she could not establish that her POTS diagnosis in 2013 was caused by molecular mimicry resulting from the Hep B vaccine she received in June 2011. The Special Master stated that as of June 2011 or shortly thereafter there was "no evidence that she was experiencing an autoimmune process at all." *Id.* at 46. The Special Master stated that under petitioner's proposed causation theory, which linked the vaccine to an autoimmune version of POTS, petitioner would have had an autoimmune reaction to the Hep B vaccine not long after the June 2, 2011 vaccination. *Id.* However, the Special Master found that there were no "lab tests suggesting the presence of inflammation, or contemporaneous treater speculation about the character of her symptoms[.]" *Id.* at 46-47.

The Special Master was persuaded by Dr. Low's testimony that if there had been an autoimmune response, there also would have been evidence of other symptoms that would have reflected an autonomic nervous system harm. Dec. at 47. Specifically, the Special Master discussed Dr. Low's testimony that if petitioner's condition was autoimmune in character, it would manifest itself through numerous concurrent

symptoms indicating autonomic nervous system harm. *Id.* at 47. The Special Master determined that petitioner could not show "that she ha[d] any of the symptoms or test results that would be associated with an autonomic neuropathy (for example, loss of bladder control). And no treater has (based on identifiable testing or other evidence) causally connected Petitioner's POTS to her vaccination," while, in contrast, "there is record evidence from close in time to the vaccination (specifically petitioner's consultations with Drs. Jarrell and Mogyoros) that rebuts any assertion of a vaccine relationship, and which is based on actual testing rather than Dr. Shoenfeld's suppositions." *Id.* Additionally, the Special Master explained, "Petitioner's theory proposes [that] the autoantibodies interfere with the norepinephrine transporter protein—but there is no corroborative evidence of *other* symptoms that this transporter was malfunctioning (beyond the fact of the POTS symptoms themselves)—and as Dr. Low observed, later testing of her norepinephrine levels did not reveal any concerns." *Id*. at 47 (emphasis in original).

Based on petitioner's medical history, the Special Master further found that petitioner failed to establish that her POTS started "close in time to the vaccination." *Id*. at 50. The Special Master concluded that the record "overwhelmingly" does not support the assertion that the Hep B vaccine contributed to petitioner's POTS symptoms, and therefore her claim based on POTS failed to satisfy the second and third *Althen* prongs. *Id*. at 48, 51.

Regarding her CFS claim, the Special Master stated that "preponderant evidence better supports Petitioner's CFS diagnosis," but petitioner did not show with a preponderance of the evidence that her CFS was caused by the Hep B vaccine. Dec. at 50. The Special Master explained that, as with POTS, petitioner had no evidence corroborating her claim that she had an autoimmune response consistent with Dr. Shoenfeld's causation theory. *Id.* at 50-51. In fact, her claim that the Hep B vaccine had caused her CFS symptoms were dismissed by her treating doctors in 2011. *Id.* at 51. For this reason and for several others, including the fact that petitioner had reported fatigue and other symptoms similar to those associated with CFS before her vaccination in 2011, the Special Master was not persuaded that she had met the preponderance of the evidence standard for *Althen* prong 2 with regard to her CFS. *Id.*

B. The Special Master Applied The Appropriate Burden of Proof

1. First *Althen* Prong

Petitioner argues that the Special Master erred by "requiring evidence that an identified homology can result in the production of specific antibodies that will cause a specific disease" on the grounds that this required petitioner to prove causation with "scientific certainty." MFR at 15.

The court finds that petitioner has misread the Special Master's decision. The Special Master required petitioner to "cite to evidence, circumstantial or otherwise, suggesting reason to find it plausible" that an autoimmune cross-reaction triggered by the Hep B vaccine could result in POTS, and in applying that requirement, the Special

Master found no reliable evidence for that theory. Dec. at 44. The standard applied by the Special Master is consistent with the requirement for "a *reputable* medical theory." *Pafford*, 451 F.3d at 1355 (emphasis added) (citation omitted). He expressly stated that he was not looking for scientific proof, but some theory that the Hep B vaccine can trigger an autoimmune response that is consistent with the unique neurological aspects of POTS. Dec. at 44.

In this connection, the Special Master's stated that molecular mimicry along with some identified homology is insufficient under *Althen* prong one in the context of petitioner's claimed injury of POTS. In finding that petitioner had not met her burden to provide a reputable theory that the Hep B vaccine can trigger an autoimmune response that can cause POTS, the Special Master identified three flaws in petitioner's theory. Dec. at 44. First, with regard to the alleged injury of POTS, the Special Master explained that petitioner's medical theory that POTS is an autoimmune illness is not a given, as Dr. Shoenfeld assumed. Choosing to rely instead on Dr. Low's testimony, one of the world's experts on POTS, the Special Master stated that he was persuaded by Dr. Low that POTS is generally not considered to be an autoimmune illness. *Id*. He noted that Dr. Low testified that the autoimmune explanation for POTS is now far less accepted and that Dr. Low does not test or treat POTS as he would an autoimmune illness. *Id.*

Second, the Special Master found that even if he accepted petitioner's theory that some forms of POTS are autoimmune in origin, petitioner's theory was not reliable because petitioner's expert, Dr. Shoenfeld, could not show *how* the Hep B vaccine could

specifically cause an autoimmune cross-reaction that could trigger POTS. Dec. at 44. The Special Master evaluated Dr. Shoenfeld's theory that the Hep B vaccine causes the production of certain antibodies and that those specific antibodies can lead to POTS. The Special Master was persuaded by the respondent's expert, Dr. Whitton, that Dr. Shoenfeld's theories were not supported. *Id.* at 44-45 ("[Dr. Whitton] similarly established convincingly that the evidence that the norepinephrine transporter protein is the target antigen for autonomic nervous system interference sufficient to result in POTS is undeveloped[.]"). The Special Master also explained that in making this determination, he considered Dr. Shoenfeld a less credible witness than Dr. Whitton.

Third, to the extent that petitioner relied on the theory of molecular mimicry along with some identified homology, the Special Master was persuaded by Dr. Whitton's testimony that identifying a homology is commonplace and of little consequence. Dec. at 44-45 ("Dr. Whitton was broadly persuasive in his points about the limited conclusions that one could draw from evidence of amino acid sequence homology (especially where, as here, it appears to have been cherry-picked to bulwark a theory, rather than discovered in studying POTS and its pathogenesis)."

In view of the foregoing, the court finds petitioner's legal claim that the Special Master misapplied *Althen* prong one is without merit. The Special Master identified the appropriate standard, properly considered the evidence, and reasonably found petitioner's theory was not reliable. The Special Master did not generally determine that homology along with molecular mimicry is insufficient under the first *Althen* prong, but rather,

where petitioner posits an autoimmune connection between the Hep B vaccine and POTS, an illness that is rarely autoimmune, if at all, petitioner needs to present a reliable theory that explains how the Hep B vaccine can cause an autoimmune response of sufficient significance as to trigger the unique neurological aspects necessary to support a diagnosis of POTS. Thus, the Special Master rationally determined that identifying a homology between the Hep B surface antigen protein and a norepinephrine transporter protein is not sufficient to present a reliable theory linking the Hep B vaccine to POTS under the first *Althen* prong where persuasive evidence had been presented showing (1) the theory that the norepinephrine transporter protein as the cause of an autoimmune reaction sufficient to cause POTS was not reputable and (2) homologies in proteins are commonplace and of little consequence.[5]

2. Second *Althen* Prong

Petitioner next argues that by searching the record for evidence of any

[5] In this connection, the court also finds that the Special Master's rejection of Dr. Shoenfeld's late-filed expert report was supported. Petitioner's counsel referenced the sixth report during oral argument, but made no argument challenging the Special Master's rejection of the report in briefing or oral argument. Oral Arg. 11:17:00-11:19:00. As such, the argument was waived. RCFC App. B, 24 (stating that the memorandum of objections must "fully and specifically state and support each objection to the decision" and "set forth any legal argument the party desires to present to the reviewing judge"). Moreover, as explained with regard to *Althen* prong two, the Special Master reasonably concluded that even if the different peptide, STIPPA, identified by Dr. Shoenfeld in his sixth report should have been accepted, it would not change the outcome. As the Special Master explained, and discussed in detail in the next section, without any corroborative evidence of symptoms or test results that would be associated with an autonomic neuropathy (for example, loss of bladder control) there was no evidence to show the vaccine caused an autoimmune response in petitioner.

autoimmune process, such as inflammation or the presence of antibodies, that the Special Master imposed a "novel requirement" on petitioner. *See* MFR at 16. Petitioner asserts that the Special Master raised the burden of proof for the second *Althen* prong by requiring "proof that an autoimmune process was occurring in June or July" [near in time to the vaccination] and proof "[that petitioner] had antibodies." *Id.* (citing Dec. at 46). The government responds that the Special Master appropriately evaluated the evidence to determine whether the evidence showed, assuming POTS and CFS can be autoimmune illnesses and petitioner had POTS and CFS, that petitioner was in fact experiencing autoimmune effects from the vaccine. Resp. at 15. The court agrees with the government that the Special Master did not elevate petitioner's burden under *Althen* prong two by requiring evidence of an autoimmune response.

The court agrees with the Special Master that where "Petitioner's theory proposes the autoantibodies interfering with the norepinephrine transporter protein" to meet *Althen* prong two, petitioner needed to offer some "corroborative evidence of *other* symptoms that this transporter was malfunctioning" besides the CFS and POTS symptoms themselves. Dec. at 47. Requiring this evidence was reasonable where the Special Master determined, based on Dr. Low's testimony, that it is unlikely that either POTS or CFS are autoimmune in nature. *Id.* at 44. Put another way, because neither POTS nor CFS are autoimmune by definition, the Special Master reasonably determined that some evidence of an autoimmune response was needed to meet the requirements of *Althen* prong two. Petitioner's counsel's argument that it is not clear what evidence of an autoimmune

process would satisfy *Althen* prong two is without merit. The Special Master indicated that if there had been an autoimmune response consistent with petitioner's theory, that he accepted Dr. Low's opinion that there should have been additional concurrent symptoms indicating autonomic nervous system harm. *Id*. at 47. Dr. Low identified those concurrent symptoms as including loss of bladder control, loss of ability to breath, and tissue injury. *Id.* at 23. The Special Master also stated that petitioner could have provided "contemporaneous treater speculation about the character of her symptoms" being autoimmune. *Id* at 47.

This is not a case where there was a lack of medical evidence and testing to establish whether petitioner had an autoimmune response. As the Special Master noted, petitioner saw many doctors following her vaccination. Dec. at 46. The Special Master stated that "Petitioner received several exams and evaluations" in the months before "any treater first acknowledged that a CFS diagnosis might be accurate" and "*none* [of the exams and evaluations] provide any corroborative evidence (particularly in the form of a test result) that would suggest she was experiencing an autoimmune process consistent with Dr. Shoenfeld's causation theory." *Id.* at 51. These exams included a rheumatologic work-up to determine if petitioner was suffering from an autoimmune illness which showed no evidence of joint inflammation or damage, and no signs to suggest inflammatory arthritis, connective tissue disorder, or evidence of a serum sickness-like disorder. *Id.* at 7 n.11. It was after the Special Master reviewed those medical records that he determined that there was "no evidence that Petitioner even *had* [antibodies consistent

with Dr. Shoenfeld's theory], and no evidence that [petitioner] was experiencing an autoimmune process at all." *Id.* at 46. The court finds no fault in the Special Master's consideration of petitioner's medical tests.

In view of the foregoing, the court finds that the Special Master's reliance on the absence of any corroborating evidence of an autonomic nervous system harm as reasonable. *Althen* prong two is aimed at tying the theoretical harm a vaccine may cause to a petitioner's illness. Because petitioner based her claim on an autoimmune response, and neither POTS nor CFS are necessarily autoimmune illnesses, it was reasonable for the Special Master to consider whether there was any corroborating evidence of an autoimmune response close in time to the vaccination. Contrary to petitioner's contentions, the Special Master did not come up with a new requirement under *Althen* prong two. The Special Master applied the appropriate standard and his factual findings under *Althen* prong two were not arbitrary and capricious because they were "based on evidence in the record" and "not wholly implausible." *See Cedillo*, 617 F.3d at 1338 (citations omitted).[6]

[6] In her motion for review, petitioner broadly alludes to an argument that the Special Master "acted arbitrarily in his review of the record evidence" without identifying any particular errors. *See* MFR at 1. This is inconsistent with the rules requiring a motion for review to identify specific errors. *See* MFR at 1; RCFC App. B, 24 (stating that the memorandum of objections must "fully and specifically state and support each objection to the decision" and "set forth any legal argument the party desires to present to the reviewing judge"). At the close of oral argument, counsel for petitioner suggested, for the first time, that the Special Master was wrong to consider petitioner's health three years prior to the vaccination and petitioner's mental health as reasons that the decision was arbitrary and capricious. *See* Oral Arg. 11:45:27-11:46:03. However, the Special Master was clear that he was not finding an alternative cause of

CONCLUSION

Because petitioner has failed to demonstrate that the Special Master applied the wrong evidentiary standard in making his findings with regard to *Althen* prongs one and two, and the court finds that the Special Master's decision is supported by substantial evidence and is not arbitrary or capricious, the petitioner's motion for review is **DENIED** and the Special Master's decision is **AFFIRMED**.

IT IS SO ORDERED.

s/Nancy B. Firestone
NANCY B. FIRESTONE
Senior Judge

petitioner's condition, *see* Dec. at 47 n.44. Moreover, because the Special Master's decision does not rest on the aforementioned considerations, they are not grounds to overturn his decision.